

0530  
0320

#4



ENTERED

OIKE

## RAW SEQUENCE LISTING

DATE: 03/18/2002

PATENT APPLICATION: US/09/903,171A

TIME: 15:37:23

Input Set : A:\510015-260.TXT

Output Set: N:\CRF3\03182002\I903171A.raw

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4 <110> APPLICANT: De Robertis, Edward M.
5   Bouwmeester, Tewis
8 <120> TITLE OF INVENTION: Endoderm, Cardiac and Neural Inducing
9   Factors
11 <130> FILE REFERENCE: 510015-260
13 <140> CURRENT APPLICATION NUMBER: US 09/903,171A
14 <141> CURRENT FILING DATE: 2001-07-11
16 <150> PRIOR APPLICATION NUMBER: US 60/020,150
17 <151> PRIOR FILING DATE: 1996-06-20
19 <160> NUMBER OF SEQ ID NOS: 10
21 <170> SOFTWARE: FastSEQ for Windows Version 3.0
23 <210> SEQ ID NO: 1
24 <211> LENGTH: 270
25 <212> TYPE: PRT
26 <213> ORGANISM: Xenopus
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30 1 5 10 15
31 Asp Gly Ala Gly Lys His Ser Glu Gly Arg Glu Arg Thr Lys Thr Tyr
32 20 25 30
33 Ser Leu Asn Ser Arg Gly Tyr Phe Arg Lys Glu Arg Gly Ala Arg Arg
34 35 40 45
35 Ser Lys Ile Leu Leu Val Asn Thr Lys Gly Leu Asp Glu Pro His Ile
36 50 55 60
37 Gly His Gly Asp Phe Gly Leu Val Ala Glu Leu Phe Asp Ser Thr Arg
38 65 70 75 80
39 Thr His Thr Asn Arg Lys Glu Pro Asp Met Asn Lys Val Lys Leu Phe
40 85 90 95
41 Ser Thr Val Ala His Gly Asn Lys Ser Ala Arg Arg Lys Ala Tyr Asn
42 100 105 110
43 Gly Ser Arg Arg Asn Ile Phe Ser Arg Arg Ser Phe Asp Lys Arg Asn
44 115 120 125
45 Thr Glu Val Thr Glu Lys Pro Gly Ala Lys Met Phe Trp Asn Asn Phe
46 130 135 140
47 Leu Val Lys Met Asn Gly Ala Pro Gln Asn Thr Ser His Gly Ser Lys
48 145 150 155 160
49 Ala Gln Glu Ile Met Lys Glu Ala Cys Lys Thr Leu Pro Phe Thr Gln
50 165 170 175
51 Asn Ile Val His Glu Asn Cys Asp Arg Met Val Ile Gln Asn Asn Leu
52 180 185 190
53 Cys Phe Gly Lys Cys Ile Ser Leu His Val Pro Asn Gln Gln Asp Arg
54 195 200 205
55 Arg Asn Thr Cys Ser His Cys Leu Pro Ser Lys Phe Thr Leu Asn His

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56      210      215      220
57 Leu Thr Leu Asn Cys Thr Gly Ser Lys Asn Val Val Lys Val Val Met
58 225      230      235      240
59 Met Val Glu Glu Cys Thr Cys Glu Ala His Lys Ser Asn Phe His Gln
60      245      250      255
61 Thr Ala Gln Phe Asn Met Asp Thr Ser Thr Thr Leu His His
62      260      265      270
64 <210> SEQ ID NO: 2
65 <211> LENGTH: 1338
66 <212> TYPE: DNA
67 <213> ORGANISM: Xenopus
69 <400> SEQUENCE: 2
70 gaattcccg caagtcgctc agaaacactg cagggctctag atatcataca atgttactaa 60
71 atgtactcag gatctgtatt atcgtctgcc ttgtgaatga tggagcagga aaacactcag 120
72 aaggacgaga aaggacaaaa acatattcac ttaacagcag aggttacttc agaaaagaaa 180
73 gaggagcacg taggagcaag attctgctgg tgaatactaa aggtcttgat gaaccccaca 240
74 ttgggcatgg tgattttcgc ttagtagctg aactatttga ttccaccaga acacatacaa 300
75 acagaaaaga gccagacatg aacaaagtca agcttttctc aacagttgcc catggaaaca 360
76 aaagtgcag aagaaaagct tacaatgggt ctagaaggaa tatttttcct cgccgttctt 420
77 ttgataaaag aaatacagag gttactgaaa agcctgggtg caagatgttc tggacaatt 480
78 ttttggttaa aatgaatgga gccccacaga atacaagcca tggcagtaaa gcacaggaaa 540
79 taatgaaaga agcttgcaaa acctgtttt tcaactcagaa tattgtacat gaaaactgtg 600
80 acaggatggt gatacagaac aatctgtgct ttggtaaatg catctctctc catgttccaa 660
81 atcagcaaga tcgacgaaat acctgttccc attgcttgcc gtccaaattt acctgaacc 720
82 acctgacgct gaattgtact ggatctaaga atgtagtaaa ggttgctcat atggtagagg 780
83 aatgcacgtg tgaagctcat aagagcaact tccaccaaac tgcacagttt aacatggata 840
84 catctactac cctgcaccat taaaggactg ccatacagta tggaaatgcc cttttgttgg 900
85 aatatttgtt acatactatg catctaaagc attatgttgc cttctatttc atataaccac 960
86 atggaataag gattgtatga attataatta acaaattggca ttttgtgtaa catgcaagat 1020
87 ctctgttcca tcagttgcaa gataaaaggc aatatttgtt tgactttttt tctacaaaat 1080
88 gaatacccaa atatatgata agataatggg gtcaaaactg ttaaggggta atgtaataat 1140
89 agggactaag tttgcccgag agcagtgacc cataacaacc aatcagcagg tatgatttac 1200
90 tggtcacctg tttaaaagca aacatcttat tggttgctat gggttactgc ttctgggcaa 1260
91 aatgtgtgcc tcataggggg gttagtgtgt tgtgtactga ataaattgta tttatttcac 1320
92 tgttacaaaa aaaaaaaaaa
94 <210> SEQ ID NO: 3
95 <211> LENGTH: 318
96 <212> TYPE: PRT
97 <213> ORGANISM: Xenopus frazzled
99 <400> SEQUENCE: 3
100 Met Ser Arg Thr Arg Lys Val Asp Ser Leu Leu Leu Leu Ala Ile Pro
101 1      5      10      15
102 Gly Leu Ala Leu Leu Leu Leu Pro Asn Ala Tyr Cys Ala Ser Cys Glu
103      20      25      30
104 Pro Val Arg Ile Pro Met Cys Lys Ser Met Pro Trp Asn Met Thr Lys
105      35      40      45
106 Met Pro Asn His Leu His His Ser Thr Gln Ala Asn Ala Ile Leu Ala
107      50      55      60
108 Ile Glu Gln Phe Glu Gly Leu Leu Thr Thr Glu Cys Ser Gln Asp Leu

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```

109 65          70          75          80
110 Leu Phe Phe Leu Cys Ala Met Tyr Ala Pro Ile Cys Thr Ile Asp Phe
111          85          90          95
112 Gln His Glu Pro Ile Lys Pro Cys Lys Ser Val Cys Glu Arg Ala Arg
113          100          105          110
114 Ala Gly Cys Glu Pro Ile Leu Ile Lys Tyr Arg His Thr Trp Pro Glu
115          115          120          125
116 Ser Leu Ala Cys Glu Glu Leu Pro Val Tyr Asp Arg Gly Val Cys Ile
117          130          135          140
118 Ser Pro Glu Ala Ile Val Thr Val Glu Gln Gly Thr Asp Ser Met Pro
119          145          150          155          160
120 Asp Phe Ser Met Asp Ser Asn Asn Gly Asn Cys Gly Ser Gly Arg Glu
121          165          170          175
122 His Cys Lys Cys Lys Pro Met Lys Ala Thr Gln Lys Thr Tyr Leu Lys
123          180          185          190
124 Asn Asn Tyr Asn Tyr Val Ile Arg Ala Lys Val Lys Glu Val Lys Val
125          195          200          205
126 Lys Cys His Asp Ala Thr Ala Ile Val Glu Val Lys Glu Ile Leu Lys
127          210          215          220
128 Ser Ser Leu Val Asn Ile Pro Lys Asp Thr Val Thr Leu Tyr Thr Asn
129          225          230          235          240
130 Ser Gly Cys Leu Cys Pro Gln Leu Val Ala Asn Glu Glu Tyr Ile Ile
131          245          250          255
132 Met Gly Tyr Glu Asp Lys Glu Arg Thr Arg Leu Leu Leu Val Glu Gly
133          260          265          270
134 Ser Leu Ala Glu Lys Trp Arg Asp Arg Leu Ala Lys Lys Val Lys Arg
135          275          280          285
136 Trp Asp Gln Lys Leu Arg Arg Pro Arg Lys Ser Lys Asp Pro Val Ala
137          290          295          300
138 Pro Ile Pro Asn Lys Asn Ser Asn Ser Arg Gln Ala Arg Ser
139          305          310          315

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141 &lt;210&gt; SEQ ID NO: 4

142 &lt;211&gt; LENGTH: 1875

143 &lt;212&gt; TYPE: DNA

144 &lt;213&gt; ORGANISM: Xenopus frazzled

146 &lt;400&gt; SEQUENCE: 4

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147 gaattccctt tcacacagga ctccctggcag aggtgaatgg ttagccctat ggatttggtt      60
148 tgttgatttt gacacatgat tgattgcttt cagataggat tgaaggactt ggatttttat      120
149 ctaattctgc acttttaa atctctgagta attgttcatt ttgtattgga tgggactaaa      180
150 gataaactta actccttgct tttgacttgc ccataaacta taagggtggg tgagttgtag      240
151 ttgcttttac atgtgccag attttccctg tattccctgt attccctcta aagtaagcct      300
152 acacatacag gttgggcaga ataacaatgt ctgcaacaag gaaagtggac tcattactgc      360
153 tactggccat acctggactg gcgcttctct tattacccaa tgcttactgt gcttcgtgtg      420
154 agcctgtgcg gatcccatg tgcaaatcta tgccatggaa catgaccaag atgcccacc      480
155 atctccacca cagcactcaa gccaatgcca tcctggcaat tgaacagttt gaaggtttgc      540
156 tgaccactga atgtagccag gaccttttgt tctttctgtg tgccatgtat gccccattt      600
157 gtaccatcga tttccagcat gaaccaatta agccttgcaa gtccgtgtgc gaaagggcca      660
158 gggccggctg tgagccatt ctcataaagt accggcacac ttggccagag agcctggcat      720
159 gtgaagagct gcccgatat gacagaggag tctgcatctc ccagaggct atcgtcacag      780

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160  tggacaacagg aacagattca atgccagact tctccatgga ttcaaacaat ggaaattgcg      840
161  gaagcggcag ggagcactgt aaatgcaagc ccatgaaggc aacccaaaag acgtatctca      900
162  agaataatta caattatgta atcagagcaa aagtgaaga ggtgaaagt aaatgccacg      960
163  acgcaacagc aattgtggaa gtaaaggaga ttctcaagtc ttccctagt aacattccta     1020
164  aagacacagt gacactgtac accaactcag gctgcttggt cccccagctt gttgccaatg     1080
165  aggaatacat aattatgggc tatgaagaca aagagcgtac caggcttcta ctagtgggaag     1140
166  gatccttggc cgaaaaatgg agagatcgct ttgctaagaa agtcaagcgc tgggatcaaa     1200
167  agcttcgacg tcccaggaaa agcaaagacc ccgtggctcc aattcccaac aaaaacagca     1260
168  attccagaca agcgcgtagt tagactaacg gaaaggtgta tggaaactct atggactttg     1320
169  aaactaagat ttgcattgtt ggaagagcaa aaaagaaatt gcactacagc acgttatatt     1380
170  ctattgttta ctacaagaag ctgggttagt tgattgtagt tctcctttcc ttcttttttt     1440
171  ttataactat atttgcacgt gttcccaggc aattgtttta ttcaacttcc agtgacagag     1500
172  cagtgactga atgtctcagc ctaaagaagc tcaattcatt tctgatcaac taatggtgac     1560
173  aagtgtttga tacttgggga aagtgaacta attgcaatgg taaatcagag aaaagttgac     1620
174  caatgttgct tttcctgtag atgaacaagt gagagatcac atttaaata tgatcacttt     1680
175  ccatttaata ctttcagcag ttttagttag atgacatgta ggatgcacct aaatctaaat     1740
176  attttatcat aaatgaagag ctgggttaga ctgtatggtc actgttggga aggtaaatgc     1800
177  ctactttgtc aattctgttt taaaaattgc ctaaataaat attaagtcct aaataaaaaa     1860
178  aaaaaaaaaa aaaaaa                                     1875
180 <210> SEQ ID NO: 5
181 <211> LENGTH: 896
182 <212> TYPE: PRT
183 <213> ORGANISM: Xenopus
185 <400> SEQUENCE: 5
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187    1          5          10          15
188  Val Leu Gln Thr Asp Cys Glu Ile Ala Gln Tyr Tyr Ile Asp Glu Glu
189          20          25          30
190  Glu Pro Pro Gly Thr Val Ile Ala Val Leu Ser Gln His Ser Ile Phe
191          35          40          45
192  Asn Thr Thr Asp Ile Pro Ala Thr Asn Phe Arg Leu Met Lys Gln Phe
193          50          55          60
194  Asn Asn Ser Leu Ile Gly Val Arg Glu Ser Asp Gly Gln Leu Ser Ile
195          65          70          75          80
196  Met Glu Arg Ile Asp Arg Glu Gln Ile Cys Arg Gln Ser Leu His Cys
197          85          90          95
198  Asn Leu Ala Leu Asp Val Val Ser Phe Ser Lys Gly His Phe Lys Leu
199          100         105         110
200  Leu Asn Val Lys Val Glu Val Arg Asp Ile Asn Asp His Ser Pro His
201          115         120         125
202  Phe Pro Ser Glu Ile Met His Val Glu Val Ser Glu Ser Ser Ser Val
203          130         135         140
204  Gly Thr Arg Ile Pro Leu Glu Ile Ala Ile Asp Glu Asp Val Gly Ser
205          145         150         155         160
206  Asn Ser Ile Gln Asn Phe Gln Ile Ser Asn Asn Ser His Phe Ser Ile
207          165         170         175
208  Asp Val Leu Thr Arg Ala Asp Gly Val Lys Tyr Ala Asp Leu Val Leu
209          180         185         190
210  Met Arg Glu Leu Asp Arg Glu Ile Gln Pro Thr Tyr Ile Met Glu Leu

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|     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|
| 211 |     | 195 |     | 200 |     | 205 |
| 212 | Leu | Ala | Met | Asp | Gly | Gly |
| 213 |     | 210 |     | 215 |     | 220 |
| 214 | Asn | Ile | Arg | Val | Leu | Asp |
| 215 | 225 |     |     | 230 |     | 235 |
| 216 | Ser | Thr | Ile | Ala | Val | Asp |
| 217 |     |     |     | 245 |     | 250 |
| 218 | Leu | Leu | Glu | Leu | His | Ala |
| 219 |     |     |     | 260 |     | 265 |
| 220 | Ile | Val | Tyr | Gly | Phe | Ser |
| 221 |     |     |     | 275 |     | 280 |
| 222 | Phe | Lys | Ile | Asn | Ser | Arg |
| 223 |     |     |     | 290 |     | 295 |
| 224 | Asp | Phe | Glu | Thr | Lys | Gln |
| 225 | 305 |     |     |     |     | 310 |
| 226 | Leu | Gly | Pro | Asn | Pro | Leu |
| 227 |     |     |     | 325 |     | 330 |
| 228 | Leu | Asp | Val | Asn | Asp | Asn |
| 229 |     |     |     | 340 |     | 345 |
| 230 | Thr | Val | Asn | Ala | Gly | Val |
| 231 |     |     |     | 355 |     | 360 |
| 232 | Asn | Phe | Ile | Ala | Leu | Ile |
| 233 |     |     |     | 370 |     | 375 |
| 234 | Gly | Gln | Val | Arg | Cys | Thr |
| 235 | 385 |     |     |     |     | 390 |
| 236 | Gln | Ala | Tyr | Glu | Asp | Ser |
| 237 |     |     |     | 405 |     | 410 |
| 238 | Arg | Glu | Asn | Ile | Ala | Ala |
| 239 |     |     |     | 420 |     | 425 |
| 240 | Gly | Phe | Pro | Ser | Leu | Lys |
| 241 |     |     |     | 435 |     | 440 |
| 242 | Asp | Glu | Asn | Asp | Asn | Ala |
| 243 |     |     |     | 450 |     | 455 |
| 244 | Ser | Ile | Leu | Glu | Asn | Asn |
| 245 | 465 |     |     |     |     | 470 |
| 246 | Ala | Arg | Asp | Ser | Asp | Gln |
| 247 |     |     |     | 485 |     | 490 |
| 248 | Val | Asp | Ala | Lys | Val | Met |
| 249 |     |     |     | 500 |     | 505 |
| 250 | Asp | Ala | Asp | Ser | Gly | Val |
| 251 |     |     |     | 515 |     | 520 |
| 252 | Lys | Leu | Lys | Gln | Leu | Asp |
| 253 |     |     |     | 530 |     | 535 |
| 254 | Pro | Gln | Leu | Ser | Thr | Arg |
| 255 | 545 |     |     |     |     | 550 |
| 256 | Asn | Asp | Asn | Cys | Pro | Val |
| 257 |     |     |     | 565 |     | 570 |
| 258 | Gly | Glu | Val | Leu | Leu | Pro |
| 259 |     |     |     | 580 |     | 585 |

**VERIFICATION SUMMARY**

DATE: 03/18/2002

PATENT APPLICATION: US/09/903,171A

TIME: 15:37:24

Input Set : A:\510015-260.TXT

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